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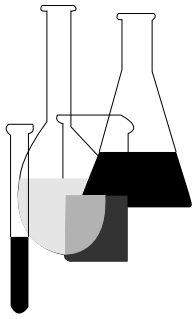
Occupational and Residential Exposure Test Guidelines

OPPTS 875.2400
Dermal Exposure



INTRODUCTION

This guideline is one of a series of test guidelines that have been developed by the Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency for use in the testing of pesticides and toxic substances, and the development of test data that must be submitted to the Agency for review under Federal regulations.

The Office of Prevention, Pesticides and Toxic Substances (OPPTS) has developed this guideline through a process of harmonization that blended the testing guidance and requirements that existed in the Office of Pollution Prevention and Toxics (OPPT) and appeared in Title 40, Chapter I, Subchapter R of the Code of Federal Regulations (CFR), the Office of Pesticide Programs (OPP) which appeared in publications of the National Technical Information Service (NTIS) and the guidelines published by the Organization for Economic Cooperation and Development (OECD).

The purpose of harmonizing these guidelines into a single set of OPPTS guidelines is to minimize variations among the testing procedures that must be performed to meet the data requirements of the U. S. Environmental Protection Agency under the Toxic Substances Control Act (15 U.S.C. 2601) and the Federal Insecticide, Fungicide and Rodenticide Act (7 U.S.C. 136, *et seq.*).

This guideline, along with the others in Series 875.2000 through 875.2900, is being substantially revised for publication in 1997. However, the current guidelines are still official. Before initiating any studies for post-application exposure registrants should contact EPA's Occupational and Residential Exposure Branch (within the Office of Pesticide Programs) at 703–305–6094.

Final Guideline Release: This guideline is available from the U.S. Government Printing Office, Washington, DC 20402 on *The Federal Bulletin Board*. By modem dial 202–512–1387, telnet and ftp: fedbbs.access.gpo.gov (IP 162.140.64.19), internet: http://fedbbs.access.gpo.gov, or call 202–512–0132 for disks or paper copies. This guideline is also available electronically in ASCII and PDF (portable document format) from the EPA Public Access Gopher (gopher.epa.gov) under the heading ''Environmental Test Methods and Guidelines.''

OPPTS 875.2400 Dermal exposure.

(a) **Scope**—(1) **Applicability.** This guideline is intended to meet testing requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136, *et seq.*).

(2) **Background.** The source material used in developing this harmonized OPPTS test guideline is OPP guideline 133–3. This guideline should be used with OPPTS 875.2000 and 875.2900.

(b) **Purpose.** (1) Use of data on dermal exposure to the pesticide or a surrogate by means of a direct exposure method is required by 40 CFR 158.l40 so that the amount of dermal exposure during the performance of an activity at a site can be estimated. The data will be used for the calculation of reentry levels and the establishment of reentry intervals as described in OPP guideline 134.

(2) If the reentry interval for a use pattern is determined by the nondetectable residue method described in OPP guideline 134–1, the data requirements of this section do not apply.

(c) **Requirements for exposure data.** (1) The purpose of this paragraph is to delineate the requirements for developing and submitting data relating to human exposure for purposes of supporting reentry intervals proposed according to OPPTS 875.2900. The registration applicant should understand that useful exposure studies using surrogate chemicals—often other pesticides—may already exist and may be cited to meet the requirements of 40 CFR 158.390. Actual conduct of the study may be unnecessary if these data are cited. Therefore, the applicant should consult with the Agency before undertaking such studies. The submission and use of extant human exposure data on a surrogate pesticide is encouraged by the Agency and is acceptable if the registrant submits descriptions demonstrating that the sites and human activities for which the surrogate exposure data were obtained produce exposure which is greater than or substantially similar to those for which the reentry interval is being proposed.

(2) A registration applicant should not undertake or authorize development of information to meet the requirements of this section in such a manner as to pose a hazard to people assigned to perform activities in the study. The Guidelines for Protection of Human Subjects (45 CFR part 46) promulgated by the U.S. Department of Health and Human Services contains information that should be considered for design of such studies. Before conducting any such studies, registration applicants should submit study protocols for approval by the appropriate institutional review board or public health department in states where the studies are to be performed.

(3) Any studies or monitoring conducted pursuant to this guideline must not violate FIFRA section 12(a)(2)(P) which provides that:

...it shall be unlawful for any person in any State to use any pesticide in tests on human beings unless such human beings (i) are fully informed of the nature and purpose of the test ..., and (ii) freely volunteer to participate in the test.

(d) **Combined studies.** (1) Direct measurement of dermal exposure to a pesticide should be combined with measurement of inhalation exposure as described in OPPTS 875.2500 when both types of data are required. The applicant should be certain that the standards for both types of studies are met.

(2) Measurement of dermal exposure to a pesticide during reentry into leafy crops should be combined with measurement of dislodgeable foliar residues. If significant exposure from soil-borne residues is expected, these measurements should be combined with quantification of soil residues. The measurement of dermal exposure may be combined with studies discussed in other guidelines, such as OPPTS Series 810 (Product Performance), OPPTS Series 850 (Hazard Evaluation: Nontarget Plants), OPPTS Series 835 and 840 (Chemistry Requirements: Environmental Fate), and OPPTS Series 860 (Chemistry Requirements: Residue Chemistry).

(e) **General test standards.** (1) The applicant should obtain data from one or more studies regarding the quantity of pesticide residues that would be expected:

(i) To be deposited on the skin and clothing of a person undertaking the maximum exposure activity upon reentry.

(ii) To be inhaled by a person undertaking the maximum exposure activity upon reentry.

(iii) To result in a dose to a person by any combined route of intake that would be appropriate for the maximum exposure activity upon reentry.

(2) Different sites may result in very similar exposures to people engaged in the same general tasks (e.g., lettuce and cabbage harvesting). If data on other pesticides indicate that this is the case, data for one site may be used to estimate exposure at another site. A detailed explanation of any extrapolation processes used, such as from published studies to the study undertaken or from studies on exposure in one crop to their use on another crop, should be reported.

(f) **Test standards.** In addition to meeting the general standards set forth in paragraph (d) of this guideline, a direct dermal exposure study should also meet the following standards:

(1) **Study substance.** A typical end-use product should be used in these studies to support registration of the pesticide.

(2) **Conduct of studies**—(i) **Attachment of exposure pads.** Dermal exposure should be assessed by use of multilayered gauze pads. Pads

should be attached to the subjects as specified in the following table 1. Each pad should be numbered so that resulting data can be related to the subject and the location of the pad on the subject.

Table 1.—Placement of exposure pads to represent exposed body areas

Body area of concern	Exposure pads representative of the body area
Face	Right and left shoulder pads
Back of neck and back ...	Back pad (upper center of the back)
Front of neck and chest	Chest pad (upper center of the chest)
Upper arms	Right and left shoulder pads and right and left forearm pads
Forearms	Right and left forearm pads (upper surface near the midpoint of each forearm)
Thighs	Right and left thigh pads (front of each thigh)
Lower legs	Right and left ankle pads (front of each ankle)

(ii) **Assessment of hand exposure.** Light cotton gloves should be used to trap residues of the pesticide or surrogate in order to develop data for assessing dermal exposure of human hands.

(iii) **Handling of samples.** Special care should be taken to protect the samples in the field. Glove and pad samples should be transported to the laboratory in sealed containers. The containers should be chilled or frozen to minimize residue losses in transit and storage.

(iv) **Typical activities.** All activities contributing to the exposure being studied should be carried out in a manner consistent with current agricultural practice.

(v) **Pesticide application**—(A) **Application rates.** Applications should be made at the maximum rate proposed for the end-use product, application method, and application situation being studied.

(B) **Application method.** Exposures should be determined after pesticide application by the method that experience has shown to

(vi) **Duration of exposure.** The exposure period should be long enough for measurable residues to be collected if exposure is occurring, but short enough to avoid excessive losses. It is impossible to specify an exact duration of exposure that will give satisfactory results for a given activity, and this factor is left to the judgment of the investigator.

(vii) **Number of replicates.** The applicant should collect dermal exposure replicates sufficient for statistical validation of the exposure. It is suggested that ten workers be monitored in a test for dermal exposure. When small test plot size makes this impossible, the number of replicates could be increased by monitoring exposure for shorter periods.

(3) **Residue extraction.** The pesticide residues should be extracted from the pads and gloves, and the extracted residues should be separated from interfering substances (e.g., by liquid chromatography) before being quantified. A study should be conducted or cited that measures the effi-

ciency of the method chosen to extract residues from exposure pads and gloves.

(4) **Residue analysis.** The residues should be quantified by a procedure capable of quantitative detection of residues on exposure pads or gloves at levels of 0.2 μg/cm² or less. A study should be conducted or cited demonstrating that the analytical procedure chosen is capable of detection at that level.

(5) **Stability of compounds**—(i) **Stability of compounds on stored pads and gloves.** If exposed pads or gloves are to be stored for longer than 24 h, a study of the stability of the residue stored on moist exposure pads and on moist gloves should be conducted under the conditions to be used for storing the field samples. The storage times should be chosen so that the longest corresponds to the longest projected storage period for field samples and so that a decay curve can be constructed to allow extrapolation of residue levels found in field samples back to the time of collection. The pads and their protective containers should be extracted and analyzed by the methods to be employed in the field studies. Storage of field samples should not exceed periods that would result in loss of 50 percent or more of the original residue.

(ii) **Stability of extracts.** If extracts from pads or gloves are to be stored for longer than 24 h before analysis, a study of stability should be conducted or cited for the solvent used. The storage times should be chosen so that the longest corresponds to the longest projected storage period for extracts from field samples and so that a decay curve can be constructed to allow extrapolation of residue levels found in stored extracts back to the time of extraction. Storage of extracts from field samples should not exceed periods that would result in loss of 50 percent or more of the residue originally extracted.

(g) **Reporting requirements.** The applicant should submit a complete description of the results of the exposure study, including all supporting data, extrapolations, estimates, and other relevant information. Such a description should include, but not be limited to:

(1) A complete description of the selected task (or tasks) used in the exposure study.

(2) A complete description of the end-use product used for the study.

(3) A complete description of the statistical approaches and treatment of data for the study.

(h) **Reporting of study results**—(1) **General site data.** The following data should be reported for each treated site where exposure data are collected:

(i) Chemical name of pesticide or surrogate.

(ii) Type of formulation.

(iii) Method of application.

(iv) Application rate.

(v) Residue levels on pertinent surfaces as listed in OPPTS 875.2100.

(vi) Dimensions of the treated site.

(vii) Environmental conditions during the exposure test.

(viii) Crop (if involved).

(ix) Activity of study subjects at the site during the exposure.

(2) **Data for individual subjects.** Each study subject should be identified by name or number. A set of field data should be compiled for each subject in the study. These data sets should be indexed so that each subject and the intensity of that subject's activity can be related to the exposure levels found. The following data should be reported for each subject:

(i) Subject identification.

(ii) Some measure of intensity or productivity of the subject's activity during exposure (e.g., pounds of fruit picked per hour).

(iii) Pad number and pad location.

(iv) Levels of toxic pesticide residues on each pad in $\mu g/cm^2/h$.

(3) **Analysis.** Laboratory operations should be recorded on a sample history sheet which should include the sample number and dates of collection, extraction, and analysis for each sample. Paired pads may be combined for extraction and residue analysis.

(4) **Calculations.** For the calculation of dermal exposures of body areas expected to be exposed during reentry activities, the human body surface areas listed in following table 2 can be used as a guide. The dermal exposure for any body area should be expressed as the product of the body surface area (see table 1) and the appropriate residue level expressed as micrograms of residue per square centimeter of exposure pad per hour of exposure. In cases where more than one pad represents the area exposed, the mean of the residues found on the appropriate pads should be used. As an example of these calculations, assume that the residue levels for a person, are as follows (in micrograms per square centimeter per hour): right shoulder, 4; left shoulder, 2; back, 3; chest, 1; right forearm, 8; and left forearm, 6; total dermal exposure for right hand, 2,000 μg and for the left hand is 1,800 μg.

Table 2.—Standard body surface areas

Body area	Body Surface area (cm^2)
Face	650
Back of neck	110
Front of neck plus "V" of chest	150
Chest and stomach	3,550
Back	3,500
Upper arms	1,320
Forearms	1,210
Hands	820
Thighs	2,250
Lower legs	2,380

These data multiplied by the adult body surface areas in table 2. gave the results shown in table 3.

Table 3.—Example of dermal exposure calculations.

Exposed area	Mean residue (μg/cm^2/h)	Skin area (cm^2) [1]	Dermal exposure (μg/h)
Face	3	650	1,950
Back of neck	3	110	330
Front of neck	1	150	150
Forearms	7	1,210	8,470
Total dermal exposure			14,700

[1] Skin areas taken from Durham and Wolfe under paragraph (i)(2) of this guideline.

(5) **Evaluation.** (i) The study results should be reported as the mean, plus or minus the standard deviation, of the exposure found for each body area for each individual in the exposure study.

(ii) Total dermal exposure should be reported in the same manner for each individual and for the study group as a whole.

(iii) For calculations, exposure below the limit of detection for the analytical method should be counted as 50 percent of that limit.

(iv) The number of individuals in the study and all assumptions used in the calculations should be specified.

(v) The results should be reported without regard to dermal absorption.

(i) **References.** The following references should be consulted for additional background material on this test guideline.

(1) Davis, J.E. Minimizing occupational exposure to pesticides: Personnel monitoring. *Residue Reviews* 75:34–50 (1980). (This review covers methodology for measurement of dermal exposure, conduct of the studies, and conversion of residue levels to total body dermal exposure.)

(2) Durham, W.F. and H.R. Wolfe. Measurement of the exposure of workers to pesticides. *Bulletin of the World Health Organization* 26:75–

91 (1962). (This paper discusses methodology for measurement of dermal exposure, conduct of the studies, and conversion of residue levels to total body exposure.)

(3) Kahn, E. Outline guide for performance of field studies to establish safe reentry intervals for organophosphate pesticides. *Residue Reviews* 70:27–44 (1979). (This paper is primarily concerned with information for development of human-subject, field study protocols for establishment of reentry intervals with organophosphorus pesticides.)